

CLAIMS

1. A pharmaceutical formulation comprising (3R,3aS,6aR)-hexahydrofuro [2,3-b] furan-3-yl (1S,2R)-3-[[(4-aminophenyl) sulfonyl] (isobutyl) amino]-1-benzyl-2-hydroxypropylcarbamate, or salt, ester, polymorphic and pseudopolymorphic form thereof; in association with a pharmaceutical carrier, said carrier comprising esters of alcohols with C₆₋₁₂ fatty acids or oils; a hydrophilic surfactant system; a hydrophilic solvent; and a nucleation inhibitor.
2. A pharmaceutical formulation comprising (3R,3aS,6aR)-hexahydrofuro [2,3-b] furan-3-yl (1S,2R)-3-[[(4-aminophenyl) sulfonyl] (isobutyl) amino]-1-benzyl-2-hydroxypropylcarbamate, or salt, ester, polymorphic and pseudopolymorphic form thereof; in association with a pharmaceutical carrier, said carrier comprising esters of alcohols with C₆₋₁₂ fatty acids or oils; a hydrophilic surfactant system; a hydrophilic solvent; and a nucleation inhibitor; characterised in that the hydrophilic solvent is in a range of 1% (w/w) to 60% (w/w), and the nucleation inhibitor is in a range of 0.1% (w/w) to 4% (w/w) of the total formulation.
3. The pharmaceutical formulation according to claim 1, wherein the esters of alcohols with C₆₋₁₂ fatty acids or oils act as a co-surfactant.
4. The pharmaceutical formulation according to claim 3, wherein the ratio between the hydrophilic surfactant system and the co-surfactant ranges between 6/4 and 9/1.
5. The pharmaceutical formulation according to any one of claims 1 to 4; wherein the esters of alcohols with C₆₋₁₂ fatty acids or oils are selected from propylene glycol monocaprylate, lauryl macrogol-32 glycerides, and mono- and diglycerides of C₈₋₁₀ fatty acids.
6. The pharmaceutical formulation according to any one of claims 1 to 5, wherein the hydrophilic surfactant system comprising a mixture of 2 surfactants in a ratio of 3:1 to 1:3.
7. The pharmaceutical formulation according to any one of claims 1 to 6, wherein the surfactants of the hydrophilic surfactant system are selected from the group of polyethylene glycol fatty acid esters; alcohol-oil transesterification products;

- polyethylene glycol glycerol fatty acid esters; polyethylene glycol sorbitan fatty acid esters; polyethylene glycol alkyl ethers; polyethylene glycol alkyl phenols; poloxamers; mono- and diglycerides, polyglycerized fatty acids; sorbitan fatty acid esters, propylene glycol fatty acid esters; lower alcohol fatty acid esters; sterol and sterol derivatives; sugar esters; and ionic surfactants.
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8. The pharmaceutical formulation according to any one of claims 1 to 7, wherein the surfactants of the hydrophilic surfactant system are selected from PEG-40 hydrogenated castor oil, d-alpha tocopheryl polyethylene glycol 1000 succinate, PEG-8 caprylic/capric glycerides, and mixtures thereof.
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9. The pharmaceutical formulation according to any one of claims 1 to 8, wherein the hydrophilic solvent is a short-chain alcohol.
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10. The pharmaceutical formulation according to any one of claims 1 to 9, wherein the nucleation inhibitor is selected from the group of synthetic products; inorganic and mineral products; modified natural polymers; natural polymers; and non-polymeric substances.
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11. The pharmaceutical formulation according to any one of claims 1 to 10, wherein the nucleation inhibitor is selected from the polyvinyl lactams having a molecular weight between 3,000 and 500,000.
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12. The pharmaceutical formulation according to any one of claims 1 to 10, which comprises the ethanolate form of (3R,3aS,6aR)-hexahydrofuro [2,3-b] furan-3-yl (1S,2R)-3-[[(4-aminophenyl) sulfonyl] (isobutyl) amino]-1-benzyl-2-hydroxypropylcarbamate; Capryol® 90; a mixture of Cremophor RH40 and Vitamin E TPGS; Transcutol®, and PVP K30.
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13. The pharmaceutical formulation according to any one of claims 1 to 12, wherein the (3R,3aS,6aR)-hexahydrofuro [2,3-b] furan-3-yl (1S,2R)-3-[[(4-aminophenyl) sulfonyl] (isobutyl) amino]-1-benzyl-2-hydroxypropylcarbamate, or salt, ester, polymorphic and pseudopolymorphic form thereof is in a range of 5% (w/w) to 50% (w/w); the esters of alcohols with C₆₋₁₂ fatty acids or oils is in a range of 2% (w/w) to 60% (w/w); the hydrophilic surfactant system is in a range of 30% (w/w) to 90% (w/w); the hydrophilic solvent is in a range of 2,9% (w/w) to 50% (w/w); and the nucleation inhibitor is in a range of 0.1% (w/w) to 4% (w/w).
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14. The pharmaceutical formulation according to any one of claims 1 to 13, wherein
the amount of (3R,3aS,6aR)-hexahydrofuro [2,3-b] furan-3-yl (1S,2R)-3-
[[(4-aminophenyl) sulfonyl] (isobutyl) amino]-1-benzyl-2-hydroxypropyl-
carbamate or salt, ester, polymorphic and pseudopolymorphic form thereof, is
5 from 50 to 800 mg per unit dose.
15. The pharmaceutical formulation according to any one of claims 1 to 14, wherein
the formulation is in a form suitable for oral administration.
- 10 16. The pharmaceutical formulation according to claim 15, wherein the form suitable
for oral administration is selected from soft gelatin capsules, hard gelatin
capsules, enteric coated soft gelatin capsules, minicapsules, and syrups.
- 15 17. A method for the treatment of HIV infected patients or suffering from AIDS,
whereby a pharmaceutical formulation according to any one of the preceding
claims is administered to a patient in the need of such treatment.